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Structural Analysis of Affinity-Matured Complexes Between T Cell Receptor V β Domains and the Superantigen *Staphylococcal enterotoxin C3*. S. Cho, M. Kerzic, E. J. Sundberg, R. Mariuzza, The Center for Advanced Research in Biotechnology, Univ. of Maryland Biotechnology Inst., Rockville, MD 20850 USA.

Molecular interactions between proteins are essential to nearly all cellular processes. Despite intensive studies, only a few structural and energetic analyses of model protein-protein interaction systems have provided useful quantitative results. We have studied a recognition system comprising mutants of a T cell receptor V β domain (TCR V β) that exhibit an overall affinity increase of \sim 1500-fold for binding to the staphylococcal enterotoxin C3 (SEC3), a bacterial superantigen that crosslinks TCR and major histocompatibility complex class II molecules to activate T cell responses. This molecular interaction has been characterized previously by scanning alanine mutagenesis, surface plasmon resonance, and microcalorimetry. However, a lack of high resolution structures of complexes in the affinity maturation pathway precluded correlations with thermodynamic data. Here we report crystal structures of mutant TCR V β /SEC3 complexes at resolutions of 2.1 Å or better, which clarify the biophysical basis for affinity maturation in this protein-protein recognition system.